NEJM Journal Watch

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Guideline Watch 2023

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Dear Reader,

Clinical guidelines are used increasingly to set practice standards and quality measures. NEJM Journal Watch not only publishes summaries of the latest clinical research, but also helps you to keep up with the guidelines most important to general medical practice.

Our physician-editors regularly survey a broad range of medical journals to identify practice guidelines from a variety of disciplines. They choose clinically impactful recommendations and highlight key points, often pointing out what's new and what remains unchanged. This collection of Guideline Watches is of broad relevance to clinical practice, spanning outpatient and inpatient medicine and addressing both primary care and subspecialty perspectives.

We hope you enjoy this compilation and find it useful for providing the best and most responsible patient care.

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Guideline Watch 2023
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Caring for Critically Ill Patients with Acute or Acute-on-Chronic Liver Failure

An SCCM guideline focuses on recommendations for critically ill patients with gastrointestinal bleeding or spontaneous bacterial peritonitis.

Patricia Kritek, MD, reviewing **Crit Care Med** 2023 May.

Sponsoring Organization: Society for Critical Care Medicine (SCCM)

Background

In 2020, the SCCM published recommendations (*Crit Care Med* 2020; 48:e173) focused on cardiovascular, hematologic, endocrine, renal, and pulmonary care of critically ill patients with acute liver failure (ALF) or acute-on-chronic liver failure (ACLF). Now, the society has published a second installment, which is focused on gastrointestinal bleeding and spontaneous bacterial peritonitis (SBP) in these patients.

Key Points

- Critically ill patients with ACLF and any form of upper gastrointestinal bleeding should be treated with prophylactic antibiotics, usually third-generation cephalosporins.
- Critically ill patients with ACLF and portal hypertensive bleeding should be treated with octreotide or a somatostatin analog (moderate-quality evidence) and a proton-pump inhibitor (low-quality evidence).
- Critically ill patients with ACLF and SBP should receive broad-spectrum empirical antibiotics, including consideration of coverage for resistant organisms.
- Patients with ACLF and SBP also should receive albumin, even if they are not clearly volume depleted, as moderate-quality evidence shows that albumin lowers risks for acute kidney injury and death.

COMMENT

The guidelines committee addressed 31 questions but felt that the evidence was only sufficient for five strong recommendations (as noted above), all of which focus on patients with ACLF. This likely reflects limited data on the care of patients with ALF (a much smaller population than ACLF). This guidance reflects what currently is common practice in most intensive care units.

Nanchal R et al. Executive Summary: Guidelines for the management of adult acute and acute-on-chronic liver failure in the ICU: Neurology, peri-transplant medicine, infectious disease, and gastroenterology considerations. **Crit Care Med** *2023 May; 51:653. (https://doi.org/10.1097/CCM.0000000000005825)*

Dr. Kritek is an Associate Editor of *NEJM Journal Watch General Medicine* and Professor of Medicine in the Division of Pulmonary, Critical Care and Sleep Medicine at the University of Washington, Seattle.

Managing Nonalcoholic Fatty Liver Disease

A new "practice guidance" document addresses diagnosis and treatment.

Allan S. Brett, MD, reviewing **Hepatology** 2023 May.

Sponsoring Organization: American Association for the Study of Liver Diseases (AASLD)

Background

The AASLD has published a new "practice guidance" document, targeted to both primary care clinicians and specialists, on clinical assessment and management of nonalcoholic fatty liver disease (NAFLD). NAFLD is an increasingly common precursor to fibrosis and cirrhosis.

Key Points

- A reminder on nomenclature: NAFLD is the umbrella term that includes both nonalcoholic fatty liver (NAFL; i.e., steatosis *without* inflammation) and nonalcoholic steatohepatitis (NASH; i.e., steatosis *with* inflammation).
- NAFLD is associated with obesity, type 2 diabetes, hypertension, and dyslipidemia; insulin resistance is a common underlying feature.
- Standard B-mode ultrasound "is not recommended as a tool to identify hepatic steatosis due to low sensitivity."
- In primary care settings, patients with risk factors for NAFLD should be screened using the fibrosis-4 (FIB-4) index, a calculation involving patient age, aspartate aminotransferase (AST), alanine aminotransferase (ALT), and platelet count. Patients with FIB-4 <1.3 are unlikely to have fibrosis and should be reassessed periodically.
- Further evaluation (e.g., by vibration-controlled transient elastography [VCTE]) should be considered for patients with FIB-4 scores >1.3. Tools such as VCTE measure liver stiffness, an indicator of fibrosis. Patients with moderate or high probability of fibrosis should be referred to a gastroenterologist or hepatologist.
- Diet and exercise — with weight reduction for overweight patients — are "the foundation of treatment" for NAFLD. Bariatric surgery has favorable effects on the natural history of NASH in selected patients (*NEJM JW Gen Med* Jun 1 2023 and *Lancet* 2023 Apr 20; [e-pub]). Patients should be encouraged to abstain from alcohol.
- No drugs are U.S. FDA approved for NASH. In studies conducted in selected patient populations, several drugs (i.e., vitamin E, pioglitazone, and glucagon-like peptide-1–receptor agonists) have shown histologic improvement of NASH, but not decisive evidence of reversal of fibrosis.

COMMENT

Patients with NAFLD are being identified increasingly in general practice — often when AST and ALT are mildly elevated on chemistry panels or when steatosis is an incidental finding on abdominal imaging. This highly readable document provides useful guidance: Each point listed above is developed in great detail. However, some clinicians might disagree with its recommendation against

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using ultrasound to evaluate patients with suspected NAFLD; a new study suggests that sensitivity of contemporary ultrasound equipment for this purpose is acceptable (NEJM JW Gen Med Jun 15 2023 and *Am J Gastroenterol* 2023; 118:840).

Rinella ME et al. AASLD practice guidance on the clinical assessment and management of nonalcoholic fatty liver disease. **Hepatology** *2023 May; 77:1797. (*https://doi.org/10.1097/HEP.0000000000000323*)*

Dr. Brett is Editor-in-Chief of NEJM Journal Watch and Clinical Professor of Medicine at the University of Colorado School of Medicine.

Consensus Statement on the Care of Heart Failure with Preserved LVEF

This document is the first to provide clinicians with guidance on caring for this population.

Frederick A. Masoudi, MD, MSPH, MACC, FAHA, reviewing **J Am Coll Cardiol** 2023 May.

Sponsoring Organization: American College of Cardiology

Background and Objective

After decades of disappointing results from trials of treatments for heart failure (HF) with preserved ejection function (HFpEF), evidence has emerged recently to guide diagnostic testing and treatment. This consensus document provides guidance for the care of this clinically challenging population.

Key Points

- The causes of dyspnea in individuals with preserved left ventricular ejection fraction (LVEF) are numerous; in addition to heart failure, noncardiac causes (e.g., lung disease) must be considered. The Universal Definition of HF requires both symptoms or signs of HF and either elevated natriuretic peptides or objective evidence of cardiogenic pulmonary or systemic congestion.
- Peripheral edema is nonspecific and can be related to decreased capillary oncotic pressure (e.g., cirrhosis, nephrosis) and noncardiac causes of increased capillary hydrostatic pressure (e.g., renal failure, portal hypertension).
- Clinical risk scores — including the H_2FPEF and the HFA-PEFF scores — can refine the estimate of the likelihood of HFpEF. The former depends upon readily available clinical data; the latter incorporates infrequently used functional testing.
- The recommended diagnostic approach in patients with dyspnea and/or edema is: a) to assess for noncardiac sources; b) apply the Universal Definition of HF; c) assess for mimics of HF (both noncardiac and cardiac), and; d) assess the likelihood of HFpEF based upon the H_2FPEF score. Notably, the document considers specific causes such as myopathic processes, valvular, or pericardial disease as HFpEF mimics.
- The cornerstone of pharmacologic management of HFpEF is sodium–glucose cotransporter-2 (SGLT-2) inhibitors, based upon randomized trials demonstrating clear and meaningful benefits of this class (*NEJM JW Cardiol* Aug 30 2021; [e-pub] and *N Engl J Med* 2021; 385:1451; *NEJM JW Cardiol* Aug 29 2022; [e-pub] and *N Engl J Med* 2022; 387:1089). Loop diuretics are used to manage volume overload. Other therapies to consider include mineralocorticoid receptor antagonists (*NEJM JW Cardiol* Apr 9 2014; [e-pub] and *N Engl J Med* 2014; 370:1383), angiotensin receptor–neprilysin inhibitors (ARNIs; *NEJM JW Cardiol* Sep 1 2019; [e-pub] and *N Engl J Med* 2019; 381:1609), or angiotensin-receptor blockers in those who cannot tolerate ARNIs, although the evidence for these treatments is not as strong as for SGLT-2 inhibitors.
- Nonpharmacological management approaches include weight loss, regular exercise, and — in higher-risk patients — the consideration of implantable pulmonary artery pressure monitoring.
- Comorbidities are common and can interact adversely with HFpEF. Those requiring particular attention include atrial fibrillation, hypertension, coronary artery disease, diabetes, chronic kidney disease, sleep apnea, and obesity.

- Because of the complexity of the population with HFpEF, collaborative care is critical. The document provides guidance for referral to cardiovascular or advanced heart failure specialists.
- The role of palliative care should be considered in many cases, although it is important to dispel any misunderstanding that palliative care is synonymous with hospice.

COMMENT

This document consolidates the evidence to diagnose and treat HFpEF into a digestible format. In addition to incorporating promising recent developments, it also highlights the substantial need for further research to optimize care for this population.

Kittleson MM et al. 2023 ACC expert consensus decision pathway on management of heart failure with preserved ejection fraction: A report of the American College of Cardiology Solution Set Oversight Committee. **J Am Coll Cardiol** *2023 May; 81:1835. (https://doi.org/10.1016/j.jacc.2023.03.393)*

Dr. Masoudi is an Associate Editor of *NEJM Journal Watch Cardiology* and Chief Science Officer and Vice President of Research and Analytics at Ascension Health.

2023 GOLD Guidelines for Chronic Obstructive Pulmonary Disease

This update to the GOLD guidelines includes new definitions of COPD and COPD exacerbation, emphasizes combined bronchodilator therapy, and minimizes use of inhaled corticosteroids.

Patricia Kritek, MD, reviewing **Am J Respir Crit Care Med** 2023 Apr 1.

Sponsoring Organization: Global Initiative for Chronic Obstructive Lung Disease (GOLD)

Background

The WHO and U.S. National Institutes for Health convened the original GOLD expert panel in 1998 to make recommendations for managing chronic obstructive pulmonary disease (COPD). GOLD now has updated its last comprehensive executive summary, published in 2017 (*NEJM JW Gen Med* Jun 15 2017 and *Am J Respir Crit Care Med* 2017; 195:557).

Key Points

- GOLD proposes a new, more-inclusive definition of COPD that focuses on respiratory symptoms, anatomic area of abnormality (airways and alveoli) and airflow obstruction as demonstrated by forced vital capacity/forced expiratory volume in 1 second (FVC/FEV1) <0.7.
- A new definition of COPD exacerbation also is included; it focuses on dyspnea or cough and sputum that worsen during ≤14 days, with associated inflammation due to airway infection, pollution, or other insult to the airways. Severity is determined by dyspnea intensity, respiratory rate, heart rate, and oxygen saturation.
- Although cigarette smoking continues to be a predominant cause of COPD, more emphasis is placed on exposure to indoor biomass smoke and air pollution in low- and middle-income countries as a risk factor.
- A new recommendation is made for chest computed tomography if patients have persistent exacerbations, symptoms out of proportion to airflow obstruction, or evidence of air trapping/hyperinflation, to reveal alternate diagnoses or target specific therapies.
- Treatments are determined by (1) degree of airflow obstruction, (2) current symptoms, (3) history of moderate and severe exacerbations, and (4) comorbidities.
- Previous treatment categories C and D have been combined into a new category, named E (for exacerbations). GOLD provides new guidance based on blood eosinophil level. Initial therapy for categories A, B, and E is as follows:
  - A: Long-acting β-agonist (LABA) or long-acting muscarinic antagonist (LAMA)
  - B: LABA + LAMA (change from monotherapy)
  - E: LABA + LAMA; if blood eosinophils are ≥300 cells/μL, consider LABA + LAMA + inhaled corticosteroid (ICS). No recommendation is made (at any eosinophil level) for ICS without combined LABA + LAMA.
  - For patients with persistent exacerbations despite LABA + LAMA + ICS or for those who have >100 eosinophils/μL, roflumilast (for patients with chronic bronchitis and FEV_1 <50% of predicted) or azithromycin (in nonsmokers) can be considered.

- Pulmonary rehabilitation is recommended for patients in treatment groups B and E.
- Recommendations for oxygen therapy, ventilatory support, and lung-volume reduction surgery are unchanged in this update, although endobronchial valve and endoscopic lung-volume reduction surgery now are included.
- Exacerbations should be treated with bronchodilators and prednisone (40 mg daily for 5 days). A 5-to-7–day course of antibiotics is appropriate for patients with increased sputum volume and purulence or for patients on mechanical ventilation.

COMMENT

Six years after the last update, the 2023 GOLD report emphasizes new definitions of both COPD and COPD exacerbation, with the former designed to be more inclusive and the latter to be more functional for clinicians. The most substantial changes to therapy are creating the "E" category, more emphasis on LABA + LAMA combination treatment for most patients, and minimizing use of ICS. A "pocket guide" to the 2023 guidelines is available online.

Agustí A et al. Global Initiative for Chronic Obstructive Lung Disease 2023 Report: GOLD executive summary. **Am J Respir Crit Care Med** *2023 Apr 1; 207:819. (https://doi.org/10.1164/rccm.202301-0106PP)*

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Managing Acute Lower Gastrointestinal Bleeding

New practice guidelines update previous recommendations on risk stratification, diagnosis, and treatment.

Rahul B. Ganatra, MD, MPH, reviewing **Am J Gastroenterol** 2023 Feb 1.

Sponsoring Organization: American College of Gastroenterology (ACG)

Background

This practice guidance updates the 2016 ACG guideline on lower gastrointestinal bleeding (LGIB; *NEJM JW Gastroenterol* Aug 2016 and *Am J Gastroenterol* 2016; 111:459). It is a systematic review using the GRADE framework to categorize strength of recommendations and quality of supporting evidence. In addition, it includes recommendations based on expert opinion (termed "key concepts"). Here, we highlight a few important recommendations.

Risk stratification:

- The previous guidelines recommended urgent (i.e., within 24 hours) colonoscopy in most patients who are hospitalized with LGIB. However, because evidence that urgent colonoscopy improves outcomes is lacking, this update emphasizes use of risk-stratification tools to aid clinical judgment in identifying patients who can undergo nonemergent or outpatient diagnostic evaluation safely.
- The Oakland score (score range, 0–35) is a validated risk-stratification tool, with a score of <8 corresponding to 95% probability of safe discharge (i.e., absence of rebleeding; no requirement for blood transfusion, procedural intervention, or readmission; and no death).
- In general, patients who are low risk, whose bleeding has stopped, and who have had a high-quality colonoscopy with adequate preparation in the past year to exclude malignancy are candidates for discharge with close outpatient follow-up.

Diagnostic evaluation:

- For patients with hemodynamically unstable LGIB, computed tomography angiography (CTA) is the preferred initial test, ideally performed within 4 hours of bleeding to maximize diagnostic yield.
- For patients in whom CTA reveals active extravasation, interventional radiology referral for transcatheter arteriography and embolization of bleeding vessels generally is recommended over colonoscopy.
- Most patients hospitalized with LGIB should undergo colonoscopy; however, determining timing and location (inpatient vs. outpatient) is a clinical judgment informed by a patient's risk factors.

Anticoagulation and antiplatelet management:

- For patients with minimal LGIB and Oakland score <8, anticoagulation can be continued.
- For patients with LGIB that necessitates hospitalization, anticoagulation should be held on admission and typically restarted within 7 days.
- For patients with life-threatening LGIB who take warfarin and require reversal, prothrombin complex concentrate is preferred over fresh frozen plasma due to superior hemostasis and faster international normalized ratio (INR) reduction.

- For patients with life-threatening LGIB who have received direct-acting oral anticoagulants (DOACs) within the past 24 hours and who remain hemodynamically unstable after initial resuscitation attempts, reversal agents (i.e., idarucizumab or andexanet alfa) should be used if available.
- Hospitalization for LGIB due to diverticular bleeding should prompt stopping aspirin (if used for primary prevention) and nonsteroidal anti-inflammatory drugs, as these impart risk for rebleeding.

COMMENT

This guideline update contains important changes from the previous version and is a worthwhile read for anyone who cares for hospitalized patients. The full article is available on the ACG website.

Sengupta N et al. Management of patients with acute lower gastrointestinal bleeding: An updated ACG guideline. **Am J Gastroenterol** *2023 Feb 1; 118:208. (https://doi.org/10.14309/ajg.0000000000002130)*

Dr. Ganatra is an Associate Editor of *NEJM Journal Watch General Medicine*; Instructor in Medicine, Harvard Medical School; and Director of Continuing Medical Education for the Medical Service, VA Boston Healthcare System.

New Practice Guidelines for Evaluating and Managing Children and Adolescents with Obesity

Evidence-based recommendations include intensive health behavior and lifestyle treatment, pharmacotherapy, and bariatric surgery.

James A. Feinstein, MD, MPH, reviewing **Pediatrics** 2023 Feb 1.

Sponsoring Organization: American Academy of Pediatrics

Background

Obesity is a complex and multifactorial disease that affects the physical and mental health of more than 14 million U.S. children and teens. The American Academy of Pediatrics released its first ever guideline to aid in the evaluation and management of pediatric obesity; guidance about obesity prevention is forthcoming.

Key Recommendations

- Any child ≥2 years old with body-mass index (BMI) ≥85th percentile should undergo a comprehensive history and physical, including evaluations of mental-behavioral health, social determinants of health, blood pressure, and age-appropriate bloodwork (e.g., lipids, alanine transaminase, glycosylated hemoglobin).
- The mainstay of management is intensive health behavior and lifestyle treatment (IHBLT), an in-person, family-based program requiring at least 26 hours of face-to-face time during 3 to 12 months.
- Pharmacotherapy can be used as an adjunct to IHBLT for selected teens ≥12 years old. Medications (e.g., metformin, orlistat, glucagon-like peptide-1 receptor agonists, topiramate) should be chosen based on indications, benefits, and risks.
- Evaluation for metabolic and bariatric surgery should be considered for teens ≥13 years old with severe obesity (BMI, ≥120% of the 95th percentile) and clinically significant comorbidities.

COMMENT

This guideline document is 100 pages long; it reads almost like a textbook on obesity, covering environmental, social, and biological factors. The bullets listed above are limited to the concrete diagnostic and therapeutic steps that have received substantial publicity — both supportive and critical.

Providing effective care for the many children with obesity whom I see each day is challenging. The biggest hurdles to initiating treatment are limited resources and long wait lists for time-intensive IHBLT. I am concerned — as are many of my colleagues — about how our healthcare system can broadly implement and pay for IHBLT, pharmacotherapy, and surgical intervention in this large patient population. And I worry about liberalizing pharmacotherapy when long-term data on efficacy and safety in children are scant.

Hampl SE et al. Clinical practice guideline for the evaluation and treatment of children and adolescents with obesity. **Pediatrics** *2023 Feb 1; 151:e2022060640. (https://doi.org/10.1542/peds.2022-060640)*

Dr. Feinstein is a Consulting Editor in Pediatrics and Adolescent Medicine for NEJM Journal Watch and an Associate Professor in the Division of General Pediatrics at the University of Colorado School of Medicine.

Treating Patients with Osteoporosis: A Focused Guideline Update

The American College of Physicians has updated its 2017 guideline.

Allan S. Brett, MD, reviewing **Ann Intern Med** 2023 Jan 3.

Sponsoring Organization: American College of Physicians (ACP)

Background

After conducting a review of the recent literature, the ACP has updated its 2017 guideline on treating patients with low bone density or osteoporosis (*NEJM JW Gen Med* Jul 15 2017 and *Ann Intern Med* 2017; 166:818). This "focused update" is limited to pharmacologic therapy; it does not address other topics such as bone-density monitoring.

Recommendations

- Bisphosphonates (i.e., alendronate and others) are recommended as first-line therapy for postmenopausal women and for men with primary osteoporosis; the recommendation is "strong" for women and "conditional" for men.
- The RANK ligand inhibitor denosumab (Prolia) is recommended as second-line therapy for women or men with contraindications to — or adverse effects from — bisphosphonates; these recommendations are "conditional" for both women and men.
- Two anabolic drugs — the sclerostin inhibitor romosozumab (Evenity) and the recombinant parathyroid hormone teriparatide (Forteo) — are recommended "conditionally" only for women with osteoporosis and very high fracture risk; these drugs are prescribed only for 1 and 2 years, respectively, and should be followed by a bisphosphonate to mitigate rebound bone loss.
- For women older than 65 with osteopenia, decisions to start bisphosphonate therapy should be individualized, according to presence of other risk factors; use of risk-assessment tools are not reviewed here.

COMMENT

This document includes a detailed review of the literature relevant to each of the drugs mentioned above, with rates of fractures prevented and adverse effects. However, an editorialist (Dr. Susan Ott) criticizes the document's lack of attention to the issue of rebound fractures after discontinuation of denosumab and argues that use of denosumab to avoid bisphosphonate side effects is a "poor choice." She also makes a case for first-line use of anabolic agents in selected patients with serious osteoporosis, particularly when less-expensive versions become available. In my view, primary care clinicians should have a look at this updated guideline, but they should also read the instructive accompanying editorial.

Qaseem A et al. Pharmacologic treatment of primary osteoporosis or low bone mass to prevent fractures in adults: A living clinical guideline from the American College of Physicians. **Ann Intern Med** *2023 Jan 3; [e-pub]. (https://doi.org/10.7326/M22-1034)*

Ott SM. Osteoporosis treatment: Not easy. **Ann Intern Med** *2023 Jan 3; [e-pub]. (https://doi.org/10.7326/M22-3580)*

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Updated KDIGO Guideline for Managing Diabetes in Patients with Chronic Kidney Disease

Newer pharmaceuticals are recommended, but expedient real-world implementation might be difficult.

Daniel D. Dressler, MD, MSc, MHM, FACP, reviewing **Ann Intern Med** 2023 Jan 10.

Sponsoring Organization: Kidney Disease: Improving Global Outcomes (KDIGO)

Background

Several years ago, KDIGO published a comprehensive guideline for managing diabetes in patients with chronic kidney disease (CKD; *NEJM JW Gen Med* Jan 15 2021 and *Ann Intern Med* 2021; 174:385). Because many new randomized trials have been published since, KDIGO has published an update that includes 13 graded recommendations and 52 "practice points" for clinicians. The updated guideline focuses particularly on sodium–glucose cotransporter-2 (SGLT-2) inhibitors, glucagon-like peptide-1 (GLP-1) receptor agonists, and the nonsteroidal mineralocorticoid-receptor antagonist finerenone.

Key Recommendations

- SGLT-2 inhibitors are recommended for patients with type 2 diabetes and CKD who have estimated glomerular filtration rates (eGFRs) ≥20 mL/minute/1.73 m^2. (The previous guideline-recommended eGFR threshold was ≥30 mL/minute.) Once started, SGLT-2 inhibitors can be continued even if eGFR falls below 20 mL/minute, unless the drug is not tolerated or renal replacement therapy is initiated. SGLT-2 inhibitors can be added for renal and cardiac protection even if diabetes is controlled with other glucose-lowering agents.
- GLP-1 receptor agonists might promote intentional weight loss in patients with obesity, diabetes, and CKD.
- The nonsteroidal mineralocorticoid-receptor antagonist finerenone is recommended for patients with type 2 diabetes and CKD (eGFR, ≥25 mL/minute) who have normal serum potassium levels and albuminuria despite a maximum tolerated dose of an angiotensin-converting–enzyme inhibitor or angiotensin-receptor blocker. Serum potassium levels should be monitored regularly after initiating this drug.

COMMENT

If these recommendations are applied broadly, they have potential to change the course of CKD progression (i.e., reducing or delaying need for renal replacement therapy) and improve other outcomes in patients with diabetes and CKD. However, editorialists astutely suggest that "structural inequalities will impede adoption," and interventions to address economic, social, and educational barriers at multiple levels are required to allow timely and affordable access to these costly, but potentially life-improving, interventions.

Navaneethan SD et al. Diabetes management in chronic kidney disease: Synopsis of the KDIGO 2022 clinical practice guideline update. **Ann Intern Med** *2023 Jan 10; [e-pub]. (https://doi.org/10.7326/M22-2904)*

Saunders M and Laiteerapong N. 2022 clinical practice guideline update for diabetes management of chronic kidney disease: An important first step, more work to do. **Ann Intern Med** *2023 Jan 10; [e-pub]. (https://doi.org/10.7326/M22-3635)*

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CHEST Perioperative Guidelines for Antithrombotic Therapy

New recommendations guide management of perioperative and periprocedural antithrombotic agents.

Daniel D. Dressler, MD, MSc, MHM, FACP, reviewing **Chest** 2023 Nov.

Sponsoring Organization: American College of Chest Physicians (ACCP)

Background

In their previous guideline on perioperative antithrombotic management (published a decade ago; *Chest* 2012;141:2 Suppl:e326S), the ACCP addressed 11 questions; now, they discuss 43 questions, using a structured approach. All recommendations are for perioperative patients who are undergoing *elective* surgery or procedures.

Key Recommendations

1. In patients who are receiving vitamin K antagonists (VKAs, e.g., warfarin) and who require VKA interruption prior to surgery:
   - Stop VKAs ≥5 days prior to surgery, and restart VKAs <24 hours following surgery.
   - Do not provide routine heparin bridging for patients who are receiving VKAs for atrial fibrillation, venous thromboembolism, or mechanical heart valves and are at low-to-moderate risk for thromboembolism. In patients at high risk for thromboembolism, consider heparin bridging.
   - For minor procedures — dental, dermatologic, ophthalmologic, pacemaker placement, and colonoscopy with or without polypectomy — VKA continuation is recommended over disruption; topical hemostatic agents (e.g., oral tranexamic acid) should be employed in appropriate settings.
2. In patients who require perioperative heparin bridging of anticoagulation therapy:
   - Stop intravenous unfractionated heparin (UFH) ≥4 hours prior to surgery, and resume UFH ≥24 hours after surgery.
   - Stop low-molecular-weight heparin (LMWH), with the last dose approximately 24 hours prior to surgery; resume LMWH ≥24 hours following surgery or procedure.
3. In patients receiving direct-acting oral anticoagulant (DOAC) therapy:
   - Based on the specific DOAC, patient factors (e.g., chronic kidney disease), individual patient bleeding risk, and expected surgical or procedural bleeding risk, stop DOACs between 1 day and 4 days prior to surgery or procedure, and resume DOACs 24 to 72 hours after surgery or procedure. Clinicians should consult the guideline for specific timing recommendations.
4. In patients receiving antiplatelet agents:
   - In general, continue aspirin perioperatively for elective noncardiac surgery. If clinicians wish to interrupt aspirin in selected patients, it should be stopped ≤7 days prior to surgery.
   - Interruption of $P2Y_{12}$ inhibitors preoperatively is based on the specific medication (i.e., clopidogrel, 5 days; ticagrelor, 3–5 days; prasugrel, 7 days). Restart agents ≤24 hours after surgery.
   - For minor procedures (e.g., dental, dermatologic, ophthalmologic), patients receiving single antiplatelet agents should continue them perioperatively, whereas patients receiving dual antiplatelet agents should continue aspirin and interrupt their $P2Y_{12}$ inhibitor.

COMMENT

Although most of the guidelines are assigned "conditional recommendation" based on low-certainty or very low–certainty evidence, the compilation provides a framework under which clinicians can offer reasonably consistent antithrombosis practices based on recently published evidence and expert opinions. The online supplement to this guideline contains an expanded introduction and methods section.

Douketis JD et al. Executive summary. Perioperative management of antithrombotic therapy: An American College of Chest Physicians clinical practice guideline. **Chest** *2022 Nov; 162:1127. (https://doi.org/10.1016/j.chest.2022.08.004)*

Douketis JD et al. Perioperative management of antithrombotic therapy: An American College of Chest Physicians clinical practice guideline. **Chest** *2022 Nov; 162:e207. (https://doi.org/10.1016/j.chest.2022.07.025)*

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CDC Recommendations for Prescribing Opioids for Pain — Continued Recalibration

The U.S. CDC reaffirmed its 2016 guideline and added more details about careful assessment of risks, benefits, and alternatives.

Thomas L. Schwenk, MD, reviewing **MMWR Recomm Rep** 2023 Nov 4.

Sponsoring Organization: U.S. Centers for Disease Control and Prevention (CDC)

Target Population: Adult outpatients with acute, subacute, and chronic pain not due to sickle cell disease, cancer, or end-of-life care.

Background

In response to what CDC authors perceived as an inaccurate and sometimes inappropriate interpretation of their 2016 Opioid Prescribing Guideline (*MMWR Recomm Rep* 2016; 65:1), the CDC has issued an updated version of the guideline. Some clinicians assumed that the previous CDC guideline was an inflexible prohibition of opioid use that would cause great harm to many patients. These updated recommendations are based on new studies that address opioid tapering and discontinuation, patient access issues, and comparisons of opioid to nonopioid and nonpharmacologic approaches to pain control.

Key Points

The CDC made 12 recommendations, described as being evidence-based, for prescribing opioids for pain; however, 7 recommendations are based on evidence described as clinical experience and studies with "major" limitations, and an additional 3 recommendations are based on evidence described as observational or randomized trials with "notable" limitations.

The recommendations provide considerable detail on the following general points:

- Nonopioid therapies should be considered first for many types of acute pain and often are preferred even for subacute and chronic pain.
- Immediate-release opioids at the lowest effective dose, and in the smallest necessary quantity, are preferred over extended-release and long-acting opioids when starting opioid therapy.
- All decisions about opioid use (i.e., initiating therapy, continuation of therapy, and changing or tapering opioid dosages) should be based on regular and detailed discussions of risks and benefits. Clinicians should access state-based prescription-monitoring programs to monitor opioid use.
- Clinicians should provide or arrange for coordinated care and appropriate use of medications (i.e., buprenorphine or methadone) for patients with opioid use disorder and should avoid termination of care or abrupt detoxification. These strategies are designed to lower risks for use of "street opioids" and overdose.
- Concurrent use of opioids and benzodiazepines should be approached with particular caution.

COMMENT

These general principles in this guideline are widely known; they generally are based on cautious and limited use of opioids at the smallest possible dose, for the shortest possible time, after detailed discussions with patients about risks, benefits, and alternatives. In an essay in the *New England Journal of Medicine*, published simultaneously with the guideline release, the guideline authors emphasize a judicious and "flexible, individualized, patient-centered" approach to opioid use.

Dowell D et al. CDC clinical practice guideline for prescribing opioids for pain — United States, 2022. **MMWR Recomm Rep** *2022 Nov 4; 71:1. (https://doi.org/10.15585/mmwr.rr7103a1)*

Dowell D et al. Prescribing opioids for pain — The new CDC clinical practice guideline. **N Engl J Med** *2022 Nov 3; [e-pub]. (https://doi.org/10.1056/NEJMp2211040)*

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Perioperative Management of Medications: Additional Guidelines

During 2021 and 2022, a multidisciplinary group has issued consensus statements on perioperative management of drugs commonly used in pulmonary, gastroenterology, neurology, psychiatry, and rheumatology practice.

Allan S. Brett, MD, reviewing **Mayo Clin Proc** 2023 Dec.

Sponsoring Organization: Society for Perioperative Assessment and Quality Improvement (SPAQI)

Background

The SPAQI has issued several "medication management consensus statements" in 2021 and 2022. Each statement provides a comprehensive overview of commonly prescribed medications (grouped by specialty) and makes recommendations on whether to continue or hold those drugs — both during the days prior to surgery and on the day of surgery. The statements can be accessed through the SPAQI website and in *Mayo Clinic Proceedings*. In 2021, NEJM Journal Watch covered the statement on endocrine and urologic medications (*NEJM JW Gen Med* Aug 1 2021 and *Mayo Clin Proc* 2021; 96:1655). Now, we provide a snapshot of subsequent statements, published between December 2021 and August 2022

Content of the Consensus Statements

The most recent statements cover the following specialties and drug categories.

- Pulmonary: Medications for asthma, chronic obstructive pulmonary disease, pulmonary hypertension, and pulmonary fibrosis
- Gastroenterology: Acid-suppressive agents, antiemetic agents, antiviral agents for hepatitis, anticholinergic and antispasmodic agents, immunomodulators (e.g., for inflammatory bowel disease) and weight-loss drugs
- Psychiatry: Antianxiety, antidepressant, and antipsychotic drugs, as well as mood-stabilizing drugs and medications for attention-deficit/hyperactivity disorder
- Neurology: Drugs for multiple sclerosis, myasthenia gravis, Parkinson disease, Alzheimer disease, and seizure disorders
- Rheumatology: Immunosuppressive drugs and nonsteroidal anti-inflammatory drugs
- HIV: Antiretroviral drugs

COMMENT

Both outpatient-based clinicians and hospitalists will find these statements to be helpful in perioperative assessment. Each document includes both narrative discussion and tables that summarize the key points.

Pfeifer KJ et al. Preoperative management of gastrointestinal and pulmonary medications: Society for Perioperative Assessment and Quality Improvement (SPAQI) consensus statement. **Mayo Clin Proc** *2021 Dec; 96:3158. (https://doi.org/10.1016/j.mayocp.2021.08.008)*

Oprea AD et al. Preoperative management of medications for psychiatric diseases: Society for Perioperative Assessment and Quality Improvement consensus statement. **Mayo Clin Proc** *2022 Feb; 97:397. (https://doi.org/10.1016/j.mayocp.2021.11.011)*

Oprea AD et al. Preoperative management of medications for neurologic diseases: Society for Perioperative Assessment and Quality Improvement consensus statement. **Mayo Clin Proc** *2022 Feb; 97:375. (https://doi.org/10.1016/j.mayocp.2021.11.010)*

Russell LA et al. Preoperative management of medications for rheumatologic and HIV diseases: Society for Perioperative Assessment and Quality Improvement (SPAQI) consensus statement. **Mayo Clin Proc** *2022 Aug; 97:1551. (https://doi.org/10.1016/j.mayocp.2022.05.002)*

Dr. Brett is Editor-in-Chief of NEJM Journal Watch and Clinical Professor of Medicine at the University of Colorado School of Medicine.

Managing Hyperglycemia in Noncritically Ill Hospitalized Adults

This new Endocrine Society guideline update is comprehensive, but most of the recommendations are based on a low level of evidence.

Aaron J. Calderon, MD, FACP, SFHM, reviewing **J Clin Endocrinol Metab** 2022 Aug.

Sponsoring Organization: Endocrine Society

Background

In 2012, the Endocrine Society published its initial guideline on managing hyperglycemia in noncritically ill hospitalized patients (*J Clin Endocrinol Metab* 2012; 97:16). This guideline updates those recommendations.

Recommendations

- For insulin-dosing adjustments in patients with diabetes who already are being treated with insulin as outpatients, real-time continuous glucose monitoring with confirmatory bedside point-of-care blood glucose testing is suggested instead of bedside glucose testing alone. This recommendation is appropriate only if proper hospital resources and training are available.
- In patients who experience hyperglycemia (blood glucose, >140 mg/dL) in conjunction with glucocorticoids, an NPH or a basal-bolus insulin regimen is suggested.
- Inpatient diabetes education should be provided at discharge.
- In patients with hyperglycemia, with or without type 2 diabetes, insulin therapy is suggested over noninsulin therapies; noninsulin therapies can be used in stable patients with type 2 diabetes, particularly those nearing hospital discharge.
- In select patients with type 2 diabetes and mild hyperglycemia, dipeptidyl peptidase-4 (DPP-4) inhibitors with correction or scheduled insulin (basal or basal-bolus) is suggested.
- In patients with no history of diabetes with hyperglycemia, correction insulin is suggested over scheduled insulin.
- In patients with diabetes who were treated with diet or noninsulin therapies prior to admission, correction or scheduled insulin is recommended, with a glucose target of 100 to 180 mg/dL.
- In patients with insulin-managed diabetes prior to admission, continuation of home insulin regimens, adjusted for current nutritional intake, is recommended to maintain a glucose target of 100 to 180 mg/dL.

COMMENT

This is a worthwhile review for those who manage patients with diabetes in the hospital. Three additional points should be noted: First, 14 of the total 15 recommendations were categorized as being based on "low" or "very low" evidence, thus leading mostly to "suggestions" instead of strong recommendations. Second, the glucose target range of 100 to 180 mg/dL for inpatients differs from another recent guideline that recommended a glucose target range of 140 to 180 mg/dL for most patients (*Diabetes Care* 2022; 45:Suppl 1:S244). These differences are based on expert opinion, as

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no strong evidence shows that any particular target limits morbidity and mortality; from a practical standpoint, the 100-to-180-mg/dL range allows for more flexibility and realistic targeting, although avoiding hypoglycemia is of paramount importance. Third, noninsulin antidiabetic agents, such as DPP-4 inhibitors (the most well-studied noninsulin medication in hospitalized patients), is supported here for patients with mild-to-moderate hyperglycemia; DPP-4 inhibitors, compared with other noninsulin agents, are thought to have fewer adverse effects that could be problematic in acutely ill patients.

Korytkowski MT et al. Management of hyperglycemia in hospitalized adult patients in non-critical care settings: An Endocrine Society clinical practice guideline. J Clin Endocrinol Metab 2022 Aug; 107:2101. (https://doi.org/10.1210/clinem/dgac278)

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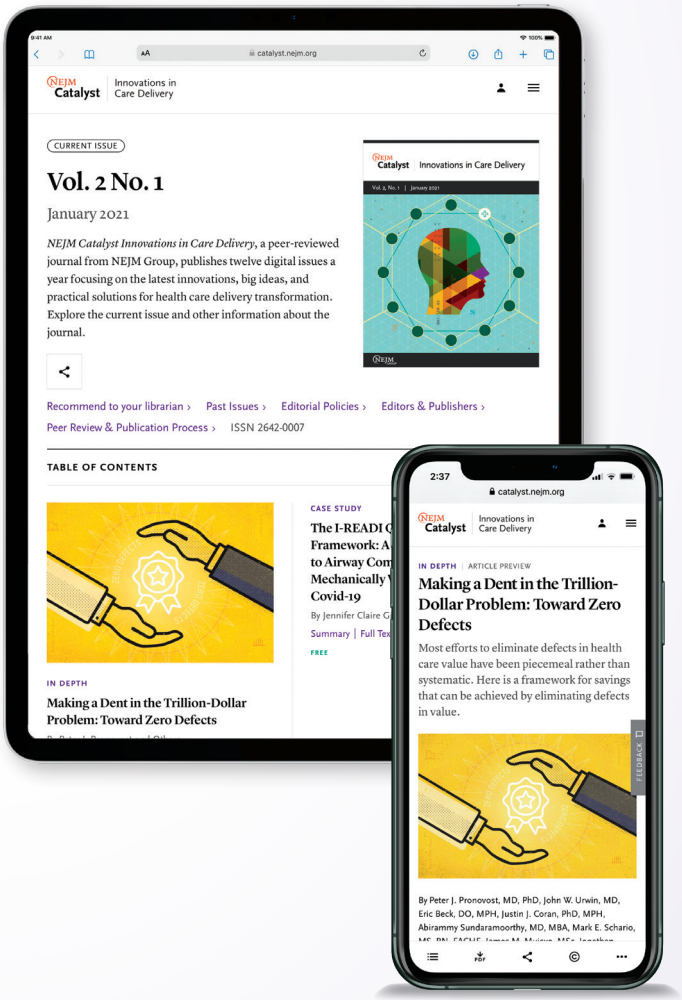
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Making a Dent in the Trillion-Dollar Problem: Toward Zero Defects
Most efforts to eliminate defects in health care value have been piecemeal rather than systematic. Here is a framework for savings that can be achieved by eliminating defects in value.
By Peter J. Pronovost, MD, PhD, John W. Urwin, MD, Eric Beck, DO, MPH, Justin J. Coran, PhD, MPH, Abirammy Sundaramoorthy, MD, MBA, Mark E. Schario,

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